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EDITORIAL COMMENT

TAVI

What Happens Behind the Stage?*

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Myocardial fibrosis (MF) is a common endpoint in most pathological mechanisms affecting cardiac muscle occurring as focal or diffuse fibrosis. Extracellular volume (ECV) is a surrogate marker for MF in several clinical scenarios, with a pivotal role in risk stratification, early diagnosis, and follow-up. Recently, cardiac magnetic resonance (CMR) has been used to detect ECV (ECV_{CMR}) as a substitute for histology.[1] However, performing CMR in the routine assessment of transcatheter aortic valve implantation (TAVI) candidates may be highly impractical because of the long acquisition time that could be challenging for patients with severe aortic stenosis (AS). Considering the clinical relevance of ECV estimation, and considering the extracellular nature of iodinated contrast, physicians started to investigate the potential role of cardiac computed tomography (CCT)-derived ECV (ECV_{CCT}). Bandula et al[2] showed good correlation between ECV_{CCT} and ECV_{CMR} by using histological quantification of MF in patients with severe AS who were surgically treated. Several papers have shown good accuracy of ECV_{CCT} in identifying subclinical cardiac amyloidosis in elderly patients with AS.[3] Baggiano et al[4] enrolled 39 consecutive patients with newly diagnosed dilated cardiomyopathy (left ventricular ejection fraction <50%) showing 100% of ECV_{CCT} evaluability with a slightly lower values compared to ECV_{CMR} (all segments, 31.8% ± 6.5% vs 33.9% ± 8.0%; $P < 0.001$). Possible explanations for slight underestimation of ECV_{CCT} include beam-hardening effects on CCT, use of vasodilator drugs before CCT acquisition, or differences in spatial resolution between CCT and CMR. In patients with AS, ECV_{cct} correlated with NYHA functional class, left atrial volume, staging classification of AS, lower left ventricular ejection fraction, and serum galectin-3 as a blood marker for fibrosis.[5] In terms of prognostic value, Tamarappoo et al[6] showed that the increase in ECV_{CCT} was associated with increased rate of mortality and hospitalization for heart failure in low-flow low-gradient AS.[6] Vignale et al[7] showed that ECV_{CCT} higher than 31.3% was associated with increased risk of death or heart failure (HR: 5.92 in patients undergoing TAVI). The greatest advantage of ECV_{CCT} is its integration into routine CCT acquisition for TAVI planning with the addition of a single acquisition post-contrast administration. It can be performed in patients with cardiac devices, and it does not require any significative modification of contrast amount. Despite these promising data, the methodology for CCT imaging acquisition and postprocessing assessment has not been standardized. Emoto et al[8] has shown that model-based iterative reconstruction improved myocardial ECV_{CCT} quantification when compared with hybrid iterative reconstruction. Recently, Koike et al[9] showed in consecutive AS patients that myocardial ECV assessment by CCT is feasible using a systolic precontrast sequential acquisition and an additional 3-minute delayed scan. Septal ECV measurement shows similar values and reproducibility to global ECV. However, the additional scan at 3 to 5 minutes determines increase of radiation dose and prolonged scan timing. To overcome this limitation, a low-dose ECV_{CCT} scan protocol was developed with a mean radiation dose 1.9 ± 0.16 mSv.[10] In addition, dual-energy computed tomography and radiomics were proposed to measure ECV form a single dataset.[11,12] Beyond ECV, assessment of myocardial motion using global longitudinal strain (GLS) with transthoracic echocardiography (TTE) is

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also of great interest. However, because of limited planes and acoustic window, image quality is often hampered in this elderly population and <60% of patients have adequate image quality.[13] Therefore, there is a growing interest in the evaluation of GLS by CCT (GLS_{CCT}) in TAVI patients. Gegenava et al[14] compared GLS_{CCT} and TTE GLS (GLS_{TTE}) in 214 consecutive TAVI patients showing an excellent correlation ($r = 0.791$, $P < 0.001$) with an underestimation by CCT as compared to TTE (mean difference of 1.44%). This underestimation could be due to lower temporal resolution of the CCT data as compared to TTE. Moreover, GLS_{TTE} is obtained from 3 apical views obtained at different beats which can introduce a small bias as compared to the isotropic nature of CCT. Also, the type of CCT scanner could play a pivotal role. The development of dual-energy computed tomography technology with superior temporal resolution has substantially improved the feasibility of GLS_{CCT} assessment from 45% in the cohort using single-source 64-slice multidetector CCT scanners up to 97%.[15] In this issue of *JACC Cardiovascular Imaging*, Koike et al[16] evaluate a comprehensive myocardial assessment pre-TAVI by CCT including ECV_{CCT} as a marker for MF and GLS_{CCT} as a marker for myocardial deformation. Over a median follow-up of 16 months, multivariable Cox proportional hazards model demonstrated that, in combination, elevated ECV_{CCT} and GLS_{CCT} showed a stronger association with the outcome (HR: 7.14; $P < 0.001$). We congratulate Koike et al[16] for this intriguing study that represents a significant step forward in the use of CCT dataset beyond the simple rule out of coronary artery disease and TAVI planning. The true novelty of this paper is the combination of ECV and GLS. Diffuse myocardial interstitial expansion and contractile dysfunction remain largely independent of one another.[17] If ECV reflects architectural distortion due to fibroblast-mediated diffuse myocardial fibrosis, GLS reflects cardiomyocyte dysfunction. In this regard, Fröjdh et al[17] has shown that ECV and GLS were minimally correlated and that, despite being both associated with outcomes, ECV carries additional prognostic value beyond GLS. Therefore, the detection of both metrics with one technique provides a more complete myocardial phenotyping, improves risk stratification, and provides personalized precision medicine. In conclusion, there is a growing interest in these 2 metrics even though several key points about ECV_{CCT} and GLS_{CCT} should continue to be investigated. We believe that the current study findings add to the body of evidence regarding the clinical relevance of CCT in patients with AS clarifying "what happen behind the stage" of TAVI patients.

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